



NOTES

SYSTEMIC MYCOSES

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Fungal infections in internal organs (esp. lungs)

CAUSES

- Dimorphic species of fungi
- Transmitted by spore inhalation; lymphohematogenous dissemination

SIGNS & SYMPTOMS

- Cough, chest pain, fever

DIAGNOSIS

DIAGNOSTIC IMAGING

- X-ray, CT scan, MRI

LAB RESULTS

- Culture-based observation, direct microscopy, serologic tests, lab tests (e.g. abnormal blood exams)

TREATMENT

MEDICATIONS

- Antifungal agents

BLASTOMYCES SPP.

osms.it/blastomyces

PATHOLOGY & CAUSES

- Blastomycosis
 - Systemic fungal infection caused by *Blastomyces dermatitidis*, *B. gilchristii*; usually manifests as chronic pneumonia
- Incubation period: 3–6 weeks
- Spore inhalation → conversion to yeast in lungs → phagocytosis by macrophages → acute suppurative inflammation
- Immune response: mainly cellular, mediated by T-lymphocytes, macrophages
- Common sites of infection: primarily lungs (90%); skin, bones, genitourinary tract, central nervous system (CNS)

Blastomyces spp.

- Size: 8–15µm
- Broad-based budding (wide connection between two cells before splitting apart during reproduction)
- Thermal dimorphism
 - Mold form (< 37°C/98.6°F): produces spores
 - Yeast form (37°C/98.6°F): multinucleate; antiphagocytic (e.g. thick cell wall)
- Virulence
 - Thick cell wall: resistance to phagocytosis
 - BAD-1: cell surface glycoprotein; adhesin
 - Binds yeast to extracellular matrix, macrophages

VISIT...

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- Blocks production of tumor necrosis factor (TNF) alpha (proinflammatory cytokine)

Clinical syndromes

- Pulmonary blastomycosis
 - Pneumonia, mostly chronic
 - Frequently affects upper lobes
- Primary cutaneous blastomycosis
 - Ulcerative/verrucous skin lesions
- Disseminated blastomycosis
 - Osteomyelitis; prostatitis, epididymo-orchitis (inflammation of epididymis/testicles); meningitis; intracranial abscesses

RISK FACTORS

- Outdoor occupations (e.g. farming)
- Recreational exposure to soil
- Immunosuppression
- High prevalence in North America
- Recent travel to endemic areas (e.g. Ohio, Mississippi river valleys)
- Comorbid conditions

COMPLICATIONS

- Acute respiratory distress, multiorgan disease, chronicity

SIGNS & SYMPTOMS

- Cough, fever, weight loss, sputum production, dyspnea, night sweats, chills, hemoptysis, arthralgia, soft tissue swelling
- **Verrucous skin lesions** with irregular borders, ulcerative skin lesions

DIAGNOSIS

DIAGNOSTIC IMAGING

X-ray

- Pneumonia
 - Lobar consolidation, alveolar infiltrates, fibronodular infiltrates, cavitation, nodules, pleural effusion
- Osteomyelitis
 - Well-defined, osteolytic bone lesions

LAB RESULTS

Culture-based observation

- tissue, sputum, body fluids
 - Sabouraud dextrose agar without cycloheximide
 - Confirmation requires conversion (mold → yeast) at 37°C/98.6°F

Direct microscopic examination

- Periodic acid–Schiff stain
- **Differentiation:** size, yeast morphology

Lab tests

- Anemia, leukocytosis, ↑ erythrocyte sedimentation rate

Tissue biopsy

- Pyogranulomatous response
- Skin
 - Epithelial hyperplasia, intraepidermal abscesses, multinucleated cells
- Fungus observation

Serologic tests

- Polymerase chain reaction (PCR)
 - Antigen detection assays

TREATMENT

MEDICATIONS

- Antifungal treatment
- Amphotericin B; followed by azole
 - **Liposomal amphotericin B:** CNS infections

SURGERY

- Resection of abscesses, devitalized bone, empyemas, pericardial effusion

COCCIDIOIDES SPP.

osms.it/coccidioides

PATHOLOGY & CAUSES

- **Coccidioidomycosis**
 - Systemic fungal infection caused by *Coccidioides immitis*, *C. posadasii*; usually manifests as acute pneumonia
- AKA San Joaquin Valley Fever/"desert rheumatism" (associated with arthralgia)
- Arthroconidium inhalation → conversion to spherules → activation of T-lymphocytes → production of cytokines → inflammation → acute pneumonia
 - In infected tissue, **spherules grow**, septate → **release endospores** → infection spreads
- Immune response
 - Mainly mediated by Th1 cells
 - Interleukin 17, TNF alpha, interferon-gamma
- **Incubation period:** 1–4 weeks
- **Common sites of infection:** lungs, skin, **bones**, CNS
- **High prevalence areas:** arid, dry regions in U.S. (e.g. **California**, **Southwest**), Mexico, Central America, South America

Coccidioides spp.

- **Size:** 20–70µm
- Dimorphism
 - **Mold form:** found in soil
 - **Yeast form:** parasitic
- Produces arthroconidia (barrel-shaped, multinucleated spores)
 - Production stimulated by human sex hormones
 - Arthroconidia convert to spherules (2–5µm; in infected tissues)
- **Infectious particles:** arthroconidia
- Virulence
 - **Enzyme with elastase activity:** ↑ infection, inflammation
 - Cell surface glycoprotein with adhesin activity

- **Metalloproteinase:** inhibits phagocytosis
- Alteration of pulmonary surfactant proteins

Clinical syndromes

- Acute pneumonia
- Dermatologic lesions
 - Wart-like lesions on face
 - Erythema nodosum/multiforme
- Osteomyelitis
- **Meningitis**

RISK FACTORS

- Outdoor occupations; recreational exposure to soil (e.g. gardening, camping); immunosuppression; recent travel to endemic areas; comorbid conditions

COMPLICATIONS

- Adult respiratory distress syndrome; fatal multilobar pneumonia; pyopneumothorax; meningitis; chronicity

SIGNS & SYMPTOMS

- Mostly mild/asymptomatic
- **Non-specific:** fever, malaise
- Cough, pleuritic pain, hemoptysis, arthralgia
- **Erythema nodosum/multiforme**
- Wart-like lesions on face (e.g. nasolabial folds)

DIAGNOSIS

DIAGNOSTIC IMAGING

X-ray

- Pneumonia
 - Parenchymal infiltrates, thin-walled cavities
- Osteomyelitis
 - Osteolytic bone lesions

LAB RESULTS

- Culture-based observation

Serologic tests

- IgM, IgG antibody detection (e.g. enzyme immunoassays)
- Antigen detection

Direct microscopic observation

- Spherules in sputum, blood, body fluid samples

Lab tests

- ↑ erythrocyte sedimentation rate
- Eosinophilia (mostly with dissemination)

Extrathoracic tissue biopsy

- Essential for diagnosis of *Coccidioides* dissemination
- Pyogranulomatous inflammation
- Presence of spherules

Spherulin skin test

- Positive after resolution; not available in U.S.

TREATMENT

MEDICATIONS

High risk of dissemination

- E.g. immunosuppression, pregnancy
 - azoles

Severe

- Amphotericin B

SURGERY

- Debridement of abscesses, devitalized bone, pyopneumothorax

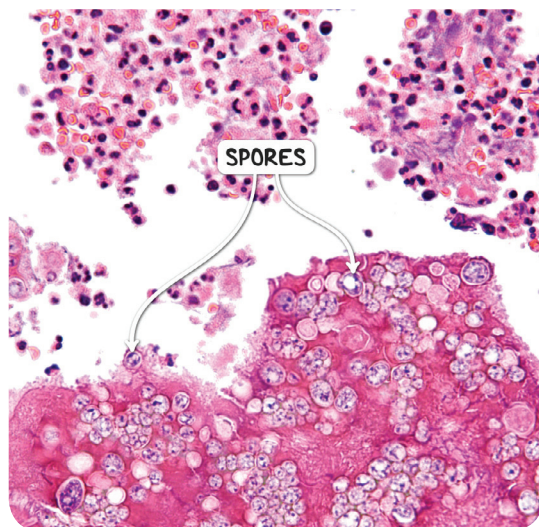


Figure 100.1 Numerous spores in the lungs of an individual with coccidioidomycosis.

HISTOPLASMA CAPSULATUM

osms.it/histoplasma-capsulatum

PATHOLOGY & CAUSES

- **Histoplasmosis**
 - Systemic fungal infection caused by *Histoplasma capsulatum*; usually manifests as acute pneumonia
- Most frequent systemic mycoses in U.S.
- Microconidia inhalation → conversion to yeast form → **macrophage** phagocytosis → inflammation → pneumonia
- **Immune response**: mainly cellular, mediated by T-lymphocytes, macrophages, TNF alpha, interferon-gamma
- **Infection sites**: primarily lungs; may disseminate to other organs

Histoplasma capsulatum

- **Size**: 2–3µm x 3–4µm
- **Thermal dimorphism**
 - Mold form (< 35°C/95°F); produces microconidia (spores, 2–5µm)
 - Yeast form (37°C/98.6°F)
- **Infectious particles**: microconidia
- **Bird, bat fecal material** promotes growth

Pulmonary histoplasmosis clinical syndromes

- **Pneumonia**: acute (diffuse/localized); chronic
- Broncholithiasis

Disseminated histoplasmosis clinical syndromes

- **Progressive disseminated histoplasmosis**: excessive reticuloendothelial infection
- Adrenal perivasculitis (common)
- Endocarditis
- Mediastinal granuloma
- Mediastinitis
- Meningitis
- Ocular histoplasmosis (e.g. retinal lesions)
- **Lesions**: intestinal (e.g. ulcers, polyps), skin (e.g. dermatitis, papules)

RISK FACTORS

- Outdoor occupations (e.g. construction, excavation)
- Outdoor activities (e.g. camping)
- Immunosuppression
- **High prevalence regions**: U.S. (**Ohio, Mississippi river valleys**), Mexico, Central America, South America
- Recent travel to endemic areas
- Comorbid conditions
- Extremes of age

COMPLICATIONS

- Fatal acute diffuse pneumonia, mediastinal granuloma, mediastinitis, chylothorax, pleural effusion

SIGNS & SYMPTOMS

- Mostly asymptomatic

Acute pulmonary histoplasmosis

- Systemic
 - Fever, headaches, fatigue
- Chest pain (pleuritic/substernal), dry cough, myalgia, arthralgia, erythema nodosum/multiforme

Chronic pulmonary histoplasmosis

- Systemic
 - Fever, fatigue, night sweats, weight loss
- Productive cough, hemoptysis, dyspnea
- **Consolidation**: dullness to percussion, crackles

DIAGNOSIS

DIAGNOSTIC IMAGING

Chest X-ray

- Hilar/mediastinal lymphadenopathy, patchy/nodular pulmonary infiltrates, occasional cavitation

LAB RESULTS

- Culture-based observation
- Direct microscopic observation

Serologic tests

- Antibody detection (e.g. immunodiffusion, complement fixation assays)
- **Antigen** detection in **urine**, sputum, body fluids (e.g. enzyme immunoassays)

Lab tests

- Anemia, ↑ erythrocyte sedimentation rate, progressive disseminated histoplasmosis (e.g. pancytopenia)

Tissue biopsy

- Granulomas, lymphohistiocytic aggregates, mononuclear cell infiltrates, fungi visualization

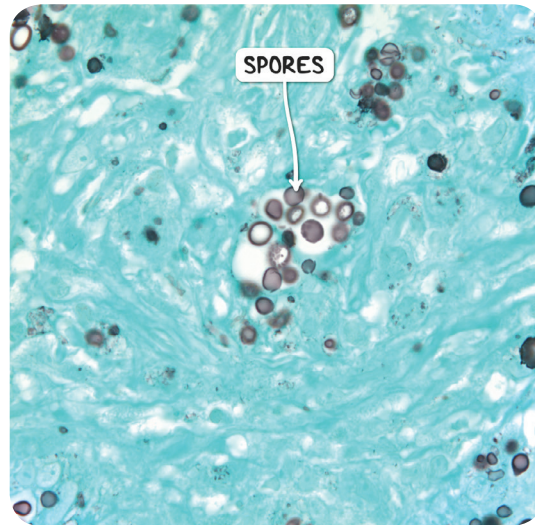


Figure 100.2 Grocott methenamine silver stain highlights spores in the lung tissue of an immunocompromised individual with histoplasmosis.

TREATMENT

MEDICATIONS

- Progressive disseminated/prolonged/severe pulmonary histoplasmosis
 - **Corticosteroids**: ↓ inflammation
 - **Antifungal treatment**: amphotericin B, azoles

PARACOCCIDIOIDES BRASILIENSIS

osms.it/paracoccidioides-brasilienses

PATHOLOGY & CAUSES

- **Paracoccidioidomycosis**
 - Systemic fungal infection caused by *Paracoccidioides brasiliensis*, *P. lutzii*; usually manifests as chronic lung disease
- AKA South American blastomycosis
- Spore inhalation → **conversion to yeast** form in lungs → phagocytosis by macrophages → inflammation → pneumonia
- **Immune response**: mostly cell-mediated
- **Common sites of infection**: mainly lungs;

oral mucosa, skin, adrenal glands, CNS

Paracoccidioides spp.

- Size: 4–40µm
- Thermal dimorphism
 - Mold form (22–26°C/71.6–78.8°F): present in soil
 - Yeast form (37°C/98.6°F): “pilot’s wheel” appearance
- Stimulated by sex hormones

Clinical syndromes

- Acute/subacute paracoccidioidomycosis (juvenile)
 - Hepatosplenomegaly,

lymphadenopathy, skin lesions, pulmonary manifestations (rare)

- Chronic paracoccidioidomycosis (adult)
 - Progressive pulmonary fibrosis (esp. lower lobes), ulcers (mouth, larynx); adrenal involvement

RISK FACTORS

- **High prevalence regions:** Central, South America (80% in Brazil)
- Outdoor occupations
- **Outdoor activities:** contact with soil
- More common in individuals who are **biologically male**
- Immunosuppression

COMPLICATIONS

- Bone marrow, adrenal dysfunction; chronic respiratory failure

SIGNS & SYMPTOMS

- Generally asymptomatic (95%)
- **Non-specific symptoms:** fever, weight loss
- Cough, dyspnea, hepatosplenomegaly, lymphadenopathies, odynophagia, sialorrhea, skin lesions (ulcers, nodules)
- **Compressive manifestations:** jaundice (bile duct obstruction)

DIAGNOSIS

DIAGNOSTIC IMAGING

X-ray/CT scan

- Acute/subacute paracoccidioidomycosis
 - Lymph node enlargement
- Chronic paracoccidioidomycosis
 - **Pulmonary disease:** alveolar/interstitial infiltrates, consolidation, masses/nodules, cavitation
 - **CNS disease:** ring enhancing lesions
 - **Articular disease:** effusion, erosions, space narrowing

LAB RESULTS

- Direct microscopic observation
- Culture-based observation



Figure 100.3 A child with numerous lesions on the face caused by *Coccidioidomycosis brasiliensis*.

Serologic tests

- Detection of antibodies through immunodiffusion

TREATMENT

MEDICATIONS

- **Antifungal treatment:** azoles
- Trimethoprim-sulfamethoxazole